Kettering Medical Center

Kettering Medical Center Network

NETWORK FACILITIES

Charles F. Kettering Memorial Hospital
3535 Southern Blvd
Kettering, Ohio 45429
(937) 298-4331

Grandview Hospital
405 Grand Ave.
Dayton, Ohio 45405
(937) 226-3200

Sycamore Hospital
2150 Leiter Rd.
Miamisburg, Ohio 45342
(937) 866-0551

Southview Hospital
1997 Miamisburg-Centerville Rd.
Dayton, Ohio 45459
(937) 439-6000

Huber Health Center
8701 Old Troy Pike
Dayton, Ohio 45424
(937) 233-8220

Kettering Youth Services
5350 Lamme Rd
Dayton, Ohio 45439
(937) 534-4600

Kettering College of Medical Arts
3737 Southern Blvd
Kettering, Ohio 45429
(937) 395-8601

Sycamore Glen Retirement Community
317 Sycamore Glen Dr.
Miamisburg, Ohio 45342
(937) 866-2984

SERVICES

Alliance Physicians
3490 Far Hills Ave
Kettering, Ohio 45429
(937) 298-9570

Wallace-Kettering Neuroscience Institute
3535 Southern Blvd
Kettering, Ohio 45429
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Kettering Cardiovascular Institute
3535 Southern Blvd
Kettering, Ohio 45429
(937) 395-8122

December 17, 2004

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Docket No. 2004N-0432

Re: Radioactive Drugs for Certain Research Uses; Public Meeting

Dear Sir or Madam:

Thank you for this opportunity to comment on the RDRC process.

Radiopharmaceuticals are diagnostic pharmaceuticals, typically they are administered only once, with no pharmacological effect on the patient. Radiopharmaceuticals have a safety profile that is unmatched by any other class of pharmaceuticals. Their unique nature needs to be the starting point for developing appropriate regulations. Trying to fit them into same or similar regulatory process as therapeutic drugs is causing a slow death of our field.

Since the inception of the RDRC process one might have expected an increase in the number of new radiopharmaceuticals that would reach the market place. Just the opposite, unfortunately has happened. Worse yet, research and development by the major radiopharmaceutical manufacturers for all practical purposes has stopped. Given the size of the nuclear medicine imaging market, the current cost of developing a new radiopharmaceutical from research bench to the imaging department is just to high. To develop a new radiopharmaceutical under the current regulatory environment is prohibitively expensive. In financial terms, there is a very poor financial return on money invested to develop new radiopharmaceuticals. Hence manufacturer's are investing their money elsewhere, not in new radiopharmaceuticals.

Revised rules for the RDRC process are necessary to help eliminate some of the financial barriers encountered during the approval process. First of all the revised rules must allow for the RDRC process to be used for clinical trials. It isn't logical to allow the use of an investigational radiopharmaceutical in a research subject for one of the current allowed uses but not for a clinical trial. How does the different use of the information generated from a study increase the risk to the research subject? The RDRC process should be the approval mechanism for Phase I and II studies. If successful, the results of these studies would then be used by the FDA during their review and evaluation of a Phase III study. I believe this would be entirely consistent with the FDA's own goals to improve translational research.

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In consideration of pharmacology issues, Andrew Taylor, MD, gave excellent recommendations at the recent RDRC meeting. A Tc-99m complex or a PET drug should be permitted to allow "first in man" studies since they can only be administered in tracer doses because of physical constraints. There is a safety factor or 1000-100,000 compared to known plant toxins. A radiopharmaceutical given in a tracer quantity, (<100 ng/kg) would be a very reasonable limit to be used by a RDRC before approving a "first in man" study. Thallium Tl-201 despite its rat poison properties, serves as excellent example of the differences between a diagnostic radiopharmaceutical and a therapeutic pharmaceutical. The regulatory approval process needs to mirror those differences.

In consideration of radiation dose limits for adult studies, Wayne L. Thompson and Henry Royal, MD, both gave the same recommendation at the recent RDRC meeting. First drop the whole body dose limit; this is an outdated method for measuring risk. Secondly drop the organ dose limits. Adopt their recommendation of using the effective dose as the most accurate method for risk estimates. The effective dose is widely recognized as the most accurate measure of total potential detriment from stochastic effects of radiation exposure.

Quality and purity standard for investigational radiopharmaceuticals should be held to chapters <797> for non <PET> drugs and 823 for PET drugs of the United States Pharmacopeia.

The membership requirements for a RDRC are appropriate and should not be changed. It has been asked if a pharmacologist or a toxicologist should be added to the committee. When appropriate these individuals can consult with the committee. To make their membership a requirement would however place a burden on some if not all committees. If membership were required, some committees such as ours would have to pay a consultant to attend all of the committee meetings. In addition, given the extraordinary safety profile of diagnostic radiopharmaceuticals, it is counter intuitive to suggest that the membership include a pharmacologist or a toxicologist.

Again I would like to thank you for this opportunity to comment on the RDRC program. Hopefully these comments and others like them will be fully embraced by the FDA in their attempts to avoid the current stagnation of drug development and to facilitate innovative new drug products to reach the market.

Sincerely,

Steve Mattmuller, BCNP, RPh
Chief Nuclear Pharmacist